Remarks

The Office Action mailed September 17, 2002, has been received and reviewed. Claims 1 through 12 and 14 through 29 are currently pending in the application, and each of claims 1 through 12 and 14 through 29 stand rejected. Claims 10, 14 and 15 are canceled herein. All claim amendments and cancellations are made without prejudice or disclaimer. Reconsideration is respectfully requested.

35 U.S.C. §112, first paragraph

Claims 1 through 10 and 16 through 21 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejection. Applicants note that claim 10 has been canceled without prejudice or disclaimer and the rejection is thus moot with respect to this claim.

Applicants have amended independent claims 1 and 2 to recite a "pair of nucleic acid probes for detection of chromosomal aberrations in hematological malignancies". Support for the amendment can be found in the as-filed specification, for example, page 9, lines 7-9. The specification further illustrates that, at the time of filing, applicants were referring to a multitude of chromosomal aberrations in hematological malignancies for which sufficient sequence information was publicly known. (Specification, pages 17 and 18 and Table 1.) Reconsideration and withdrawal of the rejection is requested.

35 U.S.C. §112, second paragraph

Claims 2 through 8, 10 through 12 and 14 through 19 stand rejected under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse the rejection. Applicants further note that claims 10, 14 and 15 have been canceled without prejudice or disclaimer and thus the rejection is moot as to these claims.

Claim 2 through 8 were allegedly indefinite for the inclusion of the phrase "from about". Applicants have amended claims 2 and 3 to remove this phrase. The phrase does not appear in dependent claims 4 through 8. Reconsideration and withdrawal of the rejection is requested.

Claims 11 and 12 were allegedly confusing because of differences between the preamble and the final step. Specifically, claim 11 recited a method for detecting a nucleic acid molecule having a chromosomal aberration while the final step recited detecting the presence of at least one different reporter molecule. Claim 12 recited a method of detecting cells suspected of having a chromosomal aberration while the final step recited detecting a different reporter signal is indicative or detecting cells suspected of having a chromosomal aberration.

Applicants have amended the method of claims 11 and 12 to recite "detecting the presence of a split signal that arises after a break within said potential breakpoint in the case of a chromosomal aberration". Reconsideration and withdrawal of the rejection is requested.

Claims 22 through 29 were rejected as being allegedly confusing because the preamble recited a method for detecting a break within a potential breakpoint of a single chromosome while the final step recited determining whether a split signal is present. Applicants have amended independent claim 22 to recite "determining whether a split-signal that arises after a break within said potential breakpoint in the case of a chromosomal aberration is present in said sample". Dependent claims 23 through 29 do not appear to contain the rejected claim language. Reconsideration and withdrawal of the rejection is requested.

35 U.S.C. § 102(b) Rejections

Claims 2 and 4 through 8 stand rejected as being anticipated by Croce (hereinafter "Croce"). Applicants respectfully traverse the rejection. Croce does not relate to hematological malignancies, but rather to solid tumors. (See, for example, Croce, abstract, col. 1, lines 20-23 and lines 61-64). Thus, claims 2 and 4 through 8 of the presently claimed invention are not anticipated by Croce. Reconsideration and withdrawal of the rejection is requested.

Conclusion

Claims 1 through 9, 11, 12 and 16 through 29 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, she is respectfully invited to contact applicants' undersigned attorney.

Respectfully submitted,

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VERSION WITH MARKINGS SHOWING CHANGES MADE

1. (Amended five times) A pair of nucleic acid probes <u>for detection of chromosomal aberrations in hematological malignancies and</u> having comparable size, said size being selected from the group consisting of from 1 to 100 kb, from 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb, and 80 to 100 kb, and flanking a potential breakpoint in a single chromosome, each of said pair of probes being labeled with at least one different reporter molecule such that a split signal arises after a break within said potential breakpoint.

2. (Amended five times) A pair of nucleic acid probes <u>for detection of chromosomal aberrations in hematological malignancies, said nucleic acid probes</u> of comparable size, said size being selected from the group consisting of from 1 to 100 kb, from 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb, and 80 to 100 kb, and flanking a potential breakpoint in a single chromosome, which pair of nucleic acid probes hybridize to a nucleic acid molecule at a genomic distance of [from about] 50 kb to no more than 100 kb.

3. (Amended four times) The pair of nucleic acid probes of comparable size of claim 1, which pair of nucleic acid probes hybridize to a nucleic acid molecule at a genomic distance of [from about] 50 kb to no more than 100 kb.

Please cancel claim 10 without prejudice or disclaimer.

11. (Amended five times) A method of detecting a nucleic acid molecule having a chromosomal aberration, said method comprising:

providing a pair of nucleic acid probes <u>to detect chromosomal aberrations in hematological malignancies and</u> to analyze a sample believed to contain said nucleic acid, said pair of nucleic acid probes having comparable size, said size being selected from the group consisting of 1 to 100 kb, 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb and 80 to 100 kb, and said pair

of nucleic acid probes flanking a potential breakpoint in a single chromosome, each of said pair of nucleic acid probes being labeled with at least one different reporter molecule;

hybridizing said pair of nucleic acid probes to said nucleic acid; and

detecting the presence of [said at least one different reporter molecule] a split signal that arises after a break within said potential breakpoint in the case of a chromosomal aberration.

12. (Amended twice) A method of detecting cells suspected of having a chromosomal aberration, said method comprising:

providing a pair of nucleic acid probes to detect chromosomal aberrations in hematological malignancies and to analyze nucleic acid of said cells, said pair of nucleic acid probes having comparable size, said size being selected from the group consisting of 1 to 100 kb, 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb and 80 to 100 kb, and said pair of nucleic acid probes flanking a potential breakpoint in a single chromosome, each of said pair of nucleic acid probes being labeled with at least one different reporter molecule;

hybridizing said pair of nucleic acid probes to the nucleic acid of at least one of said cells; and

detecting the presence of [said at least one different reporter molecule] a split signal that arises after a break within said potential breakpoint in the case of a chromosomal aberration.

Please cancel claims 14 and 15 without prejudice or disclaimer.

22. (Amended) A method of detecting a break within a potential breakpoint of a single chromosome, said method comprising:

associating a pair of nucleic acid probes for detection of chromosome aberrations in hematological malignancies and a sample believed to contain nucleic acid complementary to said pair of nucleic acid probes, said pair of nucleic acid probes having comparable size, said size being selected from the group consisting of 1 to 100 kb, 1 to 10 kb, 7 to 15 kb, 10 to 20 kb, 10 to 30 kb, 20 to 40 kb, 30 to 50 kb, 40 to 60 kb, 50 to 70 kb, 60 to 80 kb, 70 to 90 kb and 80 to 100 kb, each nucleic acid probe of said pair of nucleic acid probes being labeled with at least one different reporter molecule and

flanking a potential breakpoint in said single chromosome;

hybridizing said pair of nucleic acid probes to said nucleic acid; and

determining whether a split-signal that arises after a break within said potential breakpoint in the case of a chromosomal aberration is present in said sample.

23. (Amended) The pair of nucleic acid probes of claim 22 [21], which pair of nucleic acid probes hybridize to a nucleic acid molecule at a genomic distance of from about 50 kb to no more than 100 kb.

24. (Amended)The pair of nucleic acid probes of claim 22 [21], wherein the at least one reporter molecule of said at least one different report molecule is selected from the group consisting of enzymes, chromophores, fluorochromes, and haptens.

25. (Amended)The pair of nucleic acid probes of claim 24 [23], wherein the pair of nucleic acid probes hybridize to a single corresponding nucleic acid molecule.

26. (Amended)The pair of nucleic acid probes of claim 25 [24], wherein the single corresponding nucleic acid molecule is at least a fragment of a chromosome.

27. (Amended)The pair of nucleic acid probes of claim 26[25], wherein the chromosome is not aberrant.

28. (Amended)The pair of nucleic acid probes of claim 22, [21] which hybridize *in situ.*

29. (Amended) The pair of nucleic acid probes of claim 28 [27], which pair of nucleic acid probes each hybridize *in situ* to only a few linear DNA molecules per cell.